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WENDEROTH, LIND & PONACK, L.L.P.
2033 K STREET N. W.
SUITE 800
WASHINGTON, DC 20006-1021

EXAMINER	
TUNGATURTHI, PARITHOSH K	
ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,148	SAWYER ET AL.	
	Examiner	Art Unit	
	PARITHOSH K. TUNGATURTHI	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-13,16,17 and 20-27* is/are pending in the application.

4a) Of the above claim(s) *16, 17 and 20-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-13 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The applicant has timely traversed the non-final rejection in the reply filed on 11/23/2007, and a response to the arguments is set forth.

2. Claims 3, 14-15 and 18-19 have been cancelled.

3. Claims 1, 6 and 27 have been amended.

4. Claims 16, 17 and 20-26 have been withdrawn.

5. Claims 1, 2, 4-13 and 27 are under examination.

Rejections Withdrawn

6. The rejection of claims 18 and 19 under 35 U.S.C. 103(a) as being unpatentable over Mather et al (WO/2000/037503; Publication Date: 06/29/2000) in view of Kucherlapati et al (US Patent 6150584; Date Issued: 11/21/2000) and van de Winkel et al (PGPUB 20030138421; Publication Date: 07/24/2003) and Rava et al (US Patent 6720149; Date Filed 05/28/2002, Claims priority to 10/10/1999) and Kessler et al (PGPUB 20030044849; Date Filed:08/21/2002, Claims priority to 10/22/2001) is withdrawn in view of the cancellation of the claims.

Rejections Maintained

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 1, 2, 4-13 and 27 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Mather et al (WO/2000/037503; Publication Date: 06/29/2000) in view of Kucherlapati et al (US Patent 6150584; Date Issued: 11/21/2000) and van de Winkel et al (PGPUB 20030138421; Publication Date: 07/24/2003) and Rava et al (US Patent 6720149; Date Filed 05/28/2002, Claims priority to 10/10/1999) and Kessler et al (PGPUB 20030044849; Date Filed:08/21/2002, Claims priority to 10/22/2001).

The applicants argue that the claim requires immunization with a plurality of purified antigens ... Mather discloses immunizing an animal with intact cell and producing hybridomas from the animal ... Mather does not describe immunization of animals with purified antigens ... Mather differs from the claimed invention in both the immunization method and in the screening method ... Mather fails to disclose or suggest immunization of animals with a plurality of purified antigen (pages 7-9 of the response filed on 11/23/2007). The applicant further argue that Kucherlapati fails to disclose or

suggest immunization of animals with a plurality of purified antigens ... Kucherlapati focused on the production of a monoclonal antibody to a single antigen (pages 9-11 of the response filed on 11/23/2007) ... Van de winkel fails to remedy the deficiencies ... there is no discussion in Rava of the production of monoclonal antibodies (pages 11-13 of the response filed on 11/23/2007). The applicants argue one of skill in the art, based on art recognized definitions, would clearly understand that a "purified candidate antigen" is not equivalent to a whole intact cell.

The above arguments are carefully considered but are not found persuasive. The applicant is reminded that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Further, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The instant claims comprise introducing a plurality of candidate antigens into an animal, and paragraph 18 of the instant specification defines "candidate antigen" as any substance capable of inducing an immune response in an animal when that candidate antigen is introduced into the animal. Thus, since Mather et al teach the immunization

of an animal with a plurality of viable and intact cells that constitute cell surface antigens anchored to the plasma membrane, which upon immunization induce an immune response and result in antibody production; the plurality of cells expressing different cell surface antigens reads on the instantly claimed "plurality of candidate antigens". Further, paragraph 16 of the instant specification discloses that a "purified candidate antigen" is meant that the antigen is a homogenous preparation of antigen that is substantially free from any other components. Thus, since the plurality of cells that are immunized by Mather et al are free of serum, i.e. isolated and purified (please see page 8 of Mather et al for preparation of cells for immunization), the immunization of plurality of cells that constitute of cell surface antigens that induce immune response and generate monoclonal antibodies reads on the instantly claimed "immunization with a plurality of purified candidate antigens to produce a plurality of monoclonal antibodies".

In response to applicants arguments that Mather et al teaches away from the present invention in that Mather et al considers extraction of purified antigens for use as immunogens to be disadvantageous (page 8 of the response filed on 11/23/2007); the specific paragraph in Mather et al discussed by the applicant teaches that immunization of a whole extract consisting of cell surface antigens does not yield a population of monoclonal antibodies that specifically binds to such cell surface antigens, because the extraction of the surface antigens involves detergents that are known to dissemble the plasma membrane bilayer and dissociate the surface antigens from their native environment. Thus, Mather et al teach that extracting surface antigens may disrupt the native orientation of proteins and suggest against using detergents to dissemble the

plasma membrane and obtaining the cell surface antigens for immunization. However, Mather et al neither considers extraction of purified antigens for use as immunogens as disadvantageous nor teach away from the present invention.

As stated in the previous office action mailed 07/24/2007, Mather et al was used to establish that the concept of immunizing an animal with a plurality of candidate antigens, i.e. plurality of cells expressing different antigens on the cell surface, to generate a population of monoclonal antibodies directed against different antigens was known in the art. It would have been obvious to one of ordinary skill in the art and one would have been motivated to utilize such method of generating monoclonal antibodies and combine with the teachings of Kucherlapati et al, van de Winkel et al, Rava et al and Kessler et al to produce the claimed method, because Kucherlapati et al teach a method of immortalizing B cells obtained from the spleen, culturing the resulting hybridomas and screen for the secretion of antibodies of the desired specificity, in addition to preparation of high affinity monoclonal antibodies using BIAcore instrument, and because Van de Winkel et al teach generation of hybridomas producing monoclonal antibodies comprising generating immortalized cell line from a single cell suspension of splenic lymphocytes from immunized mice and screening for antibodies, and because Rava et al teach methods for concurrently processing multiple biological chip assays wherein a probe can be selected from proteins of interest and the targets can be selected from monoclonal antibodies, and because Kessler et al teaches isotyping monoclonal antibodies.

Thus, it is the combination of the cited references that would motivate one of ordinary skill in the art and based on such combination, one of ordinary skill in the art would have had a reasonable expectation of success to produce the claimed method of production of a plurality of monoclonal antibodies.

The applicants argue that there would be no motivation for the skilled person to replace immunization with whole cells in Mather et al with immunization with purified candidate antigens, because the skilled person in Mather did not know the identity of the antigens to which monoclonal antibodies were being generated, and would not therefore know what purified antigens to use for immunization in place of the whole cells. Such arguments are not found persuasive, because Mather et al does not immunize the animal with any random cell surface antigens, instead immunize the animal with a population of cells comprising cell surface antigens of a specific cell types; indicating that the antigens utilized to generate monoclonal antibodies are not random but, even though comprise a broad class of antigens, are specific to a specific cell type. Thus, one of ordinary skill in the art, in the interest of developing a method of producing a plurality of monoclonal antibodies to known antigens, would have been motivated to substitute the whole cells expressing cell surface antigens of a specific cell type with a population of specific antigens and utilize such antigens to screen for the specific monoclonal antibodies in the methods taught by Kucherlapati et al, van de Winkel et al and Rava et al. The applicant is again reminded that the teaching of Mather applied in this rejection is based on the ability of generating a plurality of monoclonal antibodies by immunizing an animal with a plurality of antigens. Such method is clearly and explicitly

taught by Mather et al and, as stated earlier, the combination of such method with the teachings taught by cited art would have led a skilled artisan to produce the claimed method of producing a plurality of monoclonal antibodies by immunizing an animal with a plurality of candidate antigens and selecting the monoclonal antigens that bind to candidate antigens.

In contrary to the applicant's arguments that the production of multiple monoclonal antibodies against multiple antigens simultaneously had not been contemplated previously, it is the examiners position that such method has been contemplated and successfully carried out by Mather et al. The argument that the present invention has the advantage that it is possible to map where on an antigen any antibody binds by screening every supernatant against multiple antigens is not found persuasive, because the instant claims are drawn to a method of producing plurality of monoclonal antibodies by immunizing an animal with a plurality of candidate antigens and not identifying the immunogenic epitopes of an antigen.

In response to the applicants arguments that "the present invention exhibits unexpected results over the cited prior art reference", the applicant is directed to MPEP 716.01 (C) I and II wherein it states that

> Objective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See, for example, In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984) ("It is well settled that unexpected results must be established by factual

> evidence." "[A]ppellants have not presented any experimental data showing that prior heat-shrinkable articles split. Due to the absence of tests comparing appellant's heat shrinkable articles with those of the closest prior art, we conclude that appellant's assertions of unexpected results constitute mere argument."). See also In re Lindner, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972); Ex parte George, 21 USPQ2d 1058 (Bd. Pat. App. & Inter. 1991).
>
> The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See MPEP § 2145 generally for case law pertinent to the consideration of applicant's rebuttal arguments.

Applicant's claimed method of producing multiple monoclonal antibodies against multiple antigens simultaneously is *prima facie* obvious to one of ordinary skill in the art because the prior art, Mather et al, teach the production of a plurality of monoclonal antibodies specific for different proteins.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references and the rejection is maintained.

Conclusion

10. No claims are allowed.

11. **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi
(571) 272-8789

/David J Blanchard/
Primary Examiner, Art Unit 1643

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	10/511,148	SAWYER ET AL.	
	Examiner	Art Unit	
	PARITHOSH K. TUNGATURTHI	1643	